

#2



OIEP

ENTERED

RAW SEQUENCE LISTING

DATE: 03/12/2002

PATENT APPLICATION: US/10/085,476

TIME: 15:11:01

Input Set : A:\IT0002PCA.TXT

Output Set: N:\CRF3\03122002\J085476.raw

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4 <110> APPLICANT: De Francesco, Raffaele
5   Tomei, Licia
6   Behrens, Sven-Erik
8 <120> TITLE OF INVENTION: METHOD FOR REPRODUCING IN VITRO THE
9   RNA-DEPENDENT RNA POLYMERASE AND TERMINAL NUCLEOTIDYL
10  TRANSFERASE ACTIVITIES ENCODED BY HEPATITIS C VIRUS (HCV)
13 <130> FILE REFERENCE: IT0002PCA
C--> 15 <140> CURRENT APPLICATION NUMBER: US/10/085,476
C--> 15 <141> CURRENT FILING DATE: 2002-02-27
15 <150> PRIOR APPLICATION NUMBER: 08/952,981
16 <151> PRIOR FILING DATE: 1998-03-23
18 <150> PRIOR APPLICATION NUMBER: PCT/IT96/00106
19 <151> PRIOR FILING DATE: 1996-05-24
21 <150> PRIOR APPLICATION NUMBER: RM95A000343
22 <151> PRIOR FILING DATE: 1995-05-25
24 <160> NUMBER OF SEQ ID NOS: 14
26 <170> SOFTWARE: FastSEQ for Windows Version 4.0
28 <210> SEQ ID NO: 1
29 <211> LENGTH: 591
30 <212> TYPE: PRT
31 <213> ORGANISM: Hepatitis C virus
33 <400> SEQUENCE: 1
34 Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys Ala Ala
35 1 5 10 15
36 Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg
37 20 25 30
38 His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg
39 35 40 45
40 Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp His Tyr
41 50 55 60
42 Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val Lys Ala
43 65 70 75 80
44 Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro His Ser
45 85 90 95
46 Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser
47 100 105 110
48 Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu Leu Glu
49 115 120 125
50 Asp Thr Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val
51 130 135 140
52 Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile
53 145 150 155 160
54 Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr

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55          165          170          175
56 Asp Val Val Ser Thr Leu Pro Gln Val Val Met Gly Ser Ser Tyr Gly
57          180          185          190
58 Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Thr Trp
59          195          200          205
60 Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe
61          210          215          220
62 Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr
63 225          230          235          240
64 Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu
65          245          250          255
66 Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln
67          260          265          270
68 Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser
69          275          280          285
70 Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg
71          290          295          300
72 Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp Leu
73 305          310          315          320
74 Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu
75          325          330          335
76 Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
77          340          345          350
78 Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
79          355          360          365
80 Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu
81          370          375          380
82 Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala
83 385          390          395          400
84 Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala
85          405          410          415
86 Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Ile
87          420          425          430
88 Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr
89          435          440          445
90 Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu
91          450          455          460
92 Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly
93 465          470          475          480
94 Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro Pro
95          485          490          495
96 Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu
97          500          505          510
98 Ser Gln Gly Gly Arg Ala Ala Thr Cys Gly Lys Tyr Leu Phe Asn Trp
99          515          520          525
100 Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala Ser Arg
101          530          535          540
102 Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser Gly Gly Asp Ile
103 545          550          555          560

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```

104 Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Leu Cys Leu
105          565          570          575
106 Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg
107          580          585          590
109 <210> SEQ ID NO: 2
110 <211> LENGTH: 2201
111 <212> TYPE: PRT
112 <213> ORGANISM: cDNA clone pCD (38-9.4)
114 <400> SEQUENCE: 2
115 Met Asp Arg Glu Met Ala Ala Ser Cys Gly Gly Ala Val Phe Val Gly
116 1          5          10          15
117 Leu Val Leu Leu Thr Leu Ser Pro Tyr Tyr Lys Val Phe Leu Ala Arg
118          20          25          30
119 Leu Ile Trp Trp Leu Gln Tyr Phe Thr Thr Arg Ala Glu Ala Asp Leu
120          35          40          45
121 His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Gly Arg Asp Ala Ile
122          50          55          60
123 Ile Leu Leu Met Cys Ala Val His Pro Glu Leu Ile Phe Asp Ile Thr
124 65          70          75          80
125 Lys Leu Leu Ile Ala Ile Leu Gly Pro Leu Met Val Leu Gln Ala Gly
126          85          90          95
127 Ile Thr Arg Val Pro Tyr Phe Val Arg Ala Gln Gly Leu Ile His Ala
128          100          105          110
129 Cys Met Leu Val Arg Lys Val Ala Gly Gly His Tyr Val Gln Met Ala
130          115          120          125
131 Phe Met Lys Leu Gly Ala Leu Thr Gly Thr Tyr Ile Tyr Asn His Leu
132          130          135          140
133 Thr Pro Leu Arg Asp Trp Pro Arg Ala Gly Leu Arg Asp Leu Ala Val
134 145          150          155          160
135 Ala Val Glu Pro Val Val Phe Ser Asp Met Glu Thr Lys Ile Ile Thr
136          165          170          175
137 Trp Gly Ala Asp Thr Ala Ala Cys Gly Asp Ile Ile Leu Gly Leu Pro
138          180          185          190
139 Val Ser Ala Arg Arg Gly Lys Glu Ile Leu Leu Gly Pro Ala Asp Ser
140          195          200          205
141 Leu Glu Gly Arg Gly Leu Arg Leu Leu Ala Pro Ile Thr Ala Tyr Ser
142          210          215          220
143 Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr Gly
144 225          230          235          240
145 Arg Asp Lys Asn Gln Val Glu Gly Glu Val Gln Val Val Ser Thr Ala
146          245          250          255
147 Thr Gln Ser Phe Leu Ala Thr Cys Val Asn Gly Val Cys Trp Thr Val
148          260          265          270
149 Tyr His Gly Ala Gly Ser Lys Thr Leu Ala Ala Pro Lys Gly Pro Ile
150          275          280          285
151 Thr Gln Met Tyr Thr Asn Val Asp Gln Asp Leu Val Gly Trp Pro Lys
152          290          295          300
153 Pro Pro Gly Ala Arg Ser Leu Thr Pro Cys Thr Cys Gly Ser Ser Asp
154 305          310          315          320

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```

155 Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile Pro Val Arg Arg Arg
156           325           330           335
157 Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro Arg Pro Val Ser Tyr Leu
158           340           345           350
159 Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys Pro Phe Gly His Ala Val
160           355           360           365
161 Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val Ala Lys Ala Val
162           370           375           380
163 Asp Phe Val Pro Val Glu Ser Met Glu Thr Thr Met Arg Ser Pro Val
164 385           390           395           400
165 Phe Thr Asp Asn Ser Ser Pro Pro Ala Val Pro Gln Ser Phe Gln Val
166           405           410           415
167 Ala His Leu His Ala Pro Thr Gly Ser Gly Lys Ser Thr Lys Val Pro
168           420           425           430
169 Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val Leu Val Leu Asn Pro Ser
170           435           440           445
171 Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His Gly
172           450           455           460
173 Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly Ala
174 465           470           475           480
175 Pro Val Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly Cys
176           485           490           495
177 Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser Thr
178           500           505           510
179 Asp Ser Thr Thr Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala Glu
180           515           520           525
181 Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro Gly
182           530           535           540
183 Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser Asn
184 545           550           555           560
185 Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Ile Glu Ala Ile
186           565           570           575
187 Arg Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys Asp
188           580           585           590
189 Glu Leu Ala Ala Lys Leu Ser Gly Leu Gly Ile Asn Ala Val Ala Tyr
190           595           600           605
191 Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ile Gly Asp Val Val
192           610           615           620
193 Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe Asp
194 625           630           635           640
195 Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe Ser
196           645           650           655
197 Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr Thr Val Pro Gln Asp Ala
198           660           665           670
199 Val Ser Arg Ser Gln Arg Arg Gly Arg Thr Gly Arg Gly Arg Arg Gly
200           675           680           685
201 Ile Tyr Arg Phe Val Thr Pro Gly Glu Arg Pro Ser Gly Met Phe Asp
202           690           695           700
203 Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr Glu

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204 705          710          715          720
205 Leu Thr Pro Ala Glu Thr Ser Val Arg Leu Arg Ala Tyr Leu Asn Thr
206          725          730          735
207 Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Ser Val
208          740          745          750
209 Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr Lys
210          755          760          765
211 Gln Ala Gly Asp Asn Phe Pro Tyr Leu Val Ala Tyr Gln Ala Thr Val
212          770          775          780
213 Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp Lys
214 785          790          795          800
215 Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu Leu
216          805          810          815
217 Tyr Arg Leu Gly Ala Val Gln Asn Glu Val Thr Leu Thr His Pro Ile
218          820          825          830
219 Thr Lys Tyr Ile Met Ala Cys Met Ser Ala Asp Leu Glu Val Val Thr
220          835          840          845
221 Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr
222          850          855          860
223 Cys Leu Thr Thr Gly Ser Val Val Ile Val Gly Arg Ile Ile Leu Ser
224 865          870          875          880
225 Gly Arg Pro Ala Ile Val Pro Asp Arg Glu Leu Leu Tyr Gln Glu Phe
226          885          890          895
227 Asp Glu Met Glu Glu Cys Ala Ser His Leu Pro Tyr Ile Glu Gln Gly
228          900          905          910
229 Met Gln Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu Gln
230          915          920          925
231 Thr Ala Thr Lys Gln Ala Glu Ala Ala Ala Pro Val Val Glu Ser Lys
232          930          935          940
233 Trp Arg Ala Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe Ile
234 945          950          955          960
235 Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn Pro
236          965          970          975
237 Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ser Ile Thr Ser Pro Leu
238          980          985          990
239 Thr Thr Gln Ser Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val Ala
240          995          1000          1005
241 Ala Gln Leu Ala Pro Pro Ser Ala Ala Ser Ala Phe Val Gly Ala Gly
242          1010          1015          1020
243 Ile Ala Gly Ala Ala Val Gly Ser Ile Gly Leu Gly Lys Val Leu Val
244 1025          1030          1035          1040
245 Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val Ala
246          1045          1050          1055
247 Phe Lys Val Met Ser Gly Glu Met Pro Ser Thr Glu Asp Leu Val Asn
248          1060          1065          1070
249 Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val Val
250          1075          1080          1085
251 Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala Val
252          1090          1095          1100

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VERIFICATION SUMMARY

DATE: 03/12/2002

PATENT APPLICATION: US/10/085,476

TIME: 15:11:02

Input Set : A:\IT0002PCA.TXT

Output Set: N:\CRF3\03122002\J085476.raw

L:15 M:270 C: Current Application Number differs, Replaced Current Application No
L:15 M:271 C: Current Filing Date differs, Replaced Current Filing Date